DEPARTMENT OF HEALTH & HUMAN SERVICES

Received 6/18/2009

Food and Drug Administration
Rockville MD 20857

JUN 16 2009

Rosemarie R. Wilk-Orescan
Senior Counsel
Novo Nordisk Inc.
100 College Road, West
Princeton, New Jersey 08540

Re: Docket Nos. FDA-2008-P-0343 and FDA-2008-P-0411

Dear Ms. Wilk-Orescan:

This letter responds to your petition for reconsideration (PRC) dated December 19, 2008, regarding the Food and Drug Administration's (FDA's) December 4, 2008, decision to deny your original citizen petition (FDA-2008-P-0343) (Original Petition) and to grant the related citizen petition submitted by Caraco Pharmaceutical Laboratories, Ltd. (Caraco) (FDA-2008-P-0411) (Caraco Petition). Your Original Petition requested that FDA refrain from approving any abbreviated new drug application (ANDA) for a repaglinide product that omits information on use of repaglinide in combination with metformin, a method of use which, according to your previously submitted patent information, was protected by Patent No. 6,667,358 (the '358 patent) and which currently appears in the labeling of the innovator product, Prandin (repaglinide). The Caraco Petition requested that FDA require that any ANDA for repaglinide that includes a section viii statement to carve out the method-of-use claim for use of repaglinide in combination with metformin also include a paragraph IV certification to address the other claims of the '358 patent.

This letter also responds to your petition for stay of action (Petition for Stay) dated December 20, 2008, requesting that FDA stay its citizen petition response in Docket Nos. FDA-2008-P-0343 and FDA-2008-P-0411, and refrain from taking any regulatory action consistent with the petition response, including granting any tentative or final approval for a generic repaglinide that omits information corresponding to the use code previously provided for the '358 patent. In the event that we deny your Petition for Stay, you request that FDA stay that decision for 3 business days to allow Novo Nordisk the opportunity to seek emergency relief from a court.

FDA has carefully considered the information submitted in your PRC, Petition for Stay, comments, and other relevant data available to the Agency. Based on our review of these materials and for the reasons described below, your PRC and Petition for Stay are denied as moot.

I. Background

In FDA's petition response dated December 4, 2008 (Citizen Petition Response), we denied your request that FDA refrain from approving any ANDA that carves out labeling corresponding to the previous use code for the '358 patent, because omission of the protected indication from the labeling of generic versions of repaglinide does not render repaglinide less safe and effective for the remaining, nonprotected conditions of use. In that same petition response, FDA granted Caraco's request that we require any ANDAs for repaglinide that include a section viii statement for the method-of-use claim for the use of repaglinide in combination with metformin to also include a paragraph IV certification to address the other claims of the '358 patent.

You request reconsideration of the Citizen Petition Response because you disagree with FDA's determination that generic repaglinide labeling that omits information corresponding to the use code that you had previously submitted will be safe and effective for the remaining, nonprotected conditions of use. You claim that labeling that carves out the use of repaglinide with metformin makes a generic repaglinide product less safe or effective for the treatment of type 2 diabetes.

On May 6, 2009, you submitted to FDA an amendment to the use code relating to the '358 patent. The use code for the '358 patent on which we based the Citizen Petition Response stated the following: "Use of repaglinide in combination with metformin to lower blood glucose." The amendment you recently submitted has changed the use code for the '358 patent listed for Prandin to "A method for improving glycemic control in adults with type 2 diabetes mellitus."[1]

II. Discussion

As mentioned in the Citizen Petition Response, the Federal Food, Drug, and Cosmetic Act (the Act) and FDA regulations allow a generic drug product to omit from its labeling an indication or other aspect of labeling that is protected by a method-of-use patent.[2] The regulations at 21 CFR 314.127(a)(7) further provide that to approve an ANDA containing proposed labeling that omits "aspects of the listed drug's labeling [because those aspects] are *protected by patent* [emphasis added]," we must find that the "differences do not render the proposed drug product less safe or effective than the listed drug for all remaining non-protected conditions of use."

FDA's role in listing patents is ministerial. FDA lists the patents submitted by the sponsor and publishes in the Orange Book the use codes that the sponsor provides. Sponsors must verify under penalty of perjury that the patent declaration represents "an accurate and complete submission of patent information" and attest that they are familiar

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[1] We note, by contrast, that the use code you have submitted for the same patent for PrandiMet continues to read "use of repaglinide in combination with metformin to lower blood glucose" (see FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book)).

[2] See 21 CFR 314.94(a)(8)(iv).

with the requirements of 21 CFR 314.53 and that their submission complies with that regulation (21 CFR 314.53(c)(2)(i)(Q)). FDA relies on the sponsors to craft an accurate and complete description of the relevant patent claims (to form the basis of the use code) and to identify the approved labeling that corresponds to those claims.[3] Because FDA lacks expertise in assessing patents, the Agency determines which labeling corresponds to a submitted patent (and thus which labeling may be available to carve out) by relying on the use code for that patent submitted by the sponsor. Because the use code for the '358 patent has changed since our issuance of the Citizen Petition Response and because our analysis and conclusions regarding labeling carveouts in that Citizen Petition Response were based on the previous use code, the factual predicate on which our previous response was based no longer applies. As a result, your PRC and Petition for Stay are denied as moot.

III. Conclusion

In light of the change in the factual circumstance regarding the use code for the '358 patent, your PRC and Petition for Stay are denied as moot.

Sincerely,

Jeffrey E. Shuren, M.D., J.D.
Associate Commissioner for
Policy and Planning

[3] See FDA Form 3542 and 3542a; see also 21 CFR 314.53(c). FDA regulations provide a procedure for persons to dispute the accuracy or relevance of patent information submitted by a sponsor (see 21 CFR 314.53(f)).